REMARKS/ARGUMENTS

Claims 1-4 and 7-23 were pending at the time of the mailing of the outstanding Office Action. Claims 1-3, 8, 10, 11 and 16-23 are withdrawn from consideration. By this amendment, no claims have been added or cancelled. Claims 4 and 7-18 have been amended.

In the Office Action of 19 March 2009, claims 4, 7, 9, and 12-15 were provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6 and 21-24 of co-pending US App. No. 10/706,717, as being unpatentable over claims 1-3, 5, 7-9 and 16-19 of co-pending US App. No. 10/596,797, as being unpatentable over claims 1-9 and 11 of co-pending US App. No. 10/908,729, as being unpatentable over claims 1-4 of co-pending US App. No. 11/221,322, and as being unpatentable over claims 1-4 of co-pending US App. No. 11/221,344. Claims 4, 7, 9, and 15 stand rejected under 35 U.S.C. § 102(b) as being anticipated by US Pat. No. 3,687,135 to Stroganov et al. (hereinafter "Stroganov"). Under 35 U.S.C. § 103(a), claims 12-14 were rejected as obvious over Stroganov. Claims 4 and 7 stand rejected as unpatentable under 35 U.S.C. § 103(a) over U.S. Pat. Pub. No. US2002/004060 to Heublein et al. (hereinafter "Heublein"). Finally, claims 9 and 15 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Heublien as applied to claims 4 and 7 and in further view of The Columbia Electronic Encyclopedia, 6th Edition, 2007.

The terminal disclaimers previously filed in response to the nonstatutory obviousness-type double patenting rejections were not accepted as being noncompliant with the requirements of 37 CFR 1.321 (b) and/or (c). The Applicants file herewith terminal disclaimers with regard to U.S. App. No. 10/706,717, U.S. App. No. 10/596,797, U.S. App. No. 10/908,729, U.S. App. No. 11/221,322, and U.S. App. No. 11/221,344 using form PTO/SB/25 as indicated. In light of these

terminal disclaimers, withdrawal of the provisional rejections of claims 4, 7, 9, and 12-15 on the ground of nonstatutory obviousness-type double patenting is requested.

In maintaining the rejection under 35 U.S.C. § 102(b), the Examiner continues to state, "The limitations in the claim of 'inhibiting the proliferation of smooth human muscle cells wherein the formulation is adapted for intravascular liberation after implantation in a vascular vessel' are not given patentable weight, since the composition of Stroganov et al. has pharmaceutical use in bone surgery, and thus would be capable of the intended use of the claimed invention." The Examiner additionally states that the previously forwarded arguments regarding adaptation for implantation in a vascular vessel, inhibition of smooth muscle proliferation and intravascular liberation are unpersuasive. The Examiner had previously stated that these limitations are drawn to an intended use and do not impart any structural limitations on the composition. However, the Examiner now alleges that the features previously discussed in the response of 2 January 2009, "(i.e., that the formulation is adapted for use as a stent) are not recited in the rejected claim(s)." This is clearly contrary to the wording of claim 4 as previously presented, which clearly recited adaptation for implantation in a vascular vessel. Indeed, this was one of the phrases to which the Examiner refused to give patentable weight. Therefore, this aspect of the rejection can summarized as one of refusing to give patentable weight to an element of the claim and then rejecting the claim in part because it does not contain the features of that exact element.

While the Applicants continue to traverse this assessment of the scope of the claims, in the interest of advancing the application, claims 4, 7, 9, and 15 have now been amended to recite an endoprosthesis, rather than a pharmaceutical formulation, adapted to be implanted in a vascular vessel. Support for this change may be found in paragraph 0045 of the specification. To

anticipate a claim, a reference must teach all elements of the claim (MPEP § 2131). It is respectfully maintained that Stroganov does not teach or suggest any type of endoprosthesis, particularly one adapted for implantation in a vascular vessel. A bone screw as disclosed by Stroganov would clearly not be considered to be the equivalent of an endoprosthesis as recited in the claims and would not be adapted for implantation in a blood vessel.

As stated previously, Stroganov provides a device that is intended and adapted for use in bone surgery, not for use in an endoprosthesis for placement in vascular vessels. Stroganov does not provide any teaching or suggestion that an alloy of this composition is suitable for implantation in a vascular vessel under any conditions, or that it may be adapted for intravascular liberation as recited in claim 4. Because Stroganov does not teach or suggest such elements, claim 4 patentably distinguishes over Stroganov.

Similarly, the assertion that the elements of claim 15 do not impart a structural limitation was repeated in the outstanding Office Action. Claim 15 additionally recites that the endoprosthesis delivers yttrium to smooth muscle cells at a concentration between 200 μM and 2 mM. It was alleged that Stroganov's composition would be capable of delivering such a concentration. However, Stroganov does not provide an endoprosthesis adapted for implantation in a vascular vessel at all. As also discussed previously, Stroganov only discloses the use of their composition for joining bone fragments and to stimulate bone growth. Stroganov does not teach or suggest the delivery of yttrium to smooth muscle cells, and therefore, Stroganov also does not teach or suggest the delivery of the specified amounts of yttrium to smooth muscle cells as recited in claim 15.

Therefore, claims 4, 7, 9, and 15 patentably distinguish over US Pat. No. 3,687,135 to Stroganov et al. Withdrawal of the rejection of these claims under 35 U.S.C. § 102(b) is respectfully requested.

Claims 9 and 12-14 stand rejected under 35 U.S.C. §103(a) as being obvious over Stroganov. It was alleged in the Office Action that a person of ordinary skill in the art would have found it obvious to arrive at the present formulations as recited in these claims based on Stroganov's disclosure.

As stated above, Stroganov does not provide an endoprosthesis adapted for implantation in a vascular vessel or adapted to inhibit the proliferation of human smooth muscle cells. As stated previously, Stroganov is silent regarding the effect of their composition on smooth muscle cells. Furthermore, Stroganov indicates that the composition actually *stimulates* the proliferation of bone tissue (Stroganov, column 2, lines 10-12). Stimulation of tissue growth in a vascular vessel would be undesirable, as likely triggering restenosis (see paragraph 0005 of specification). Therefore, if the teachings of Stroganov regarding bone tissue are extrapolated to smooth muscle tissue, one of skill in the art would have expected Stroganov's composition to stimulate cell growth instead of inhibiting it, making it undesirable as an endoprosthesis. There is no indication that one of ordinary skill in the art would have predicted an opposite reaction in smooth muscle cells from bone tissue. Therefore, Stroganov actually teaches away from use of the recited alloy compositions in an endoprosthesis by providing a composition that stimulates cell growth instead of inhibiting it. A person having ordinary skill in the art would not have had a reasonable expectation of success in using Stroganov's composition in the claimed endoprosthesis.

The Examiner has again maintained, "the teaching in Stroganov of stimulating bone growth does not exclude its compositions from being used for the inhibition of proliferation of smooth muscle cells, and Applicants have not presented objective evidence that the compositions of Stroganov would not be capable of the intended uses recited in the claimed invention." However, as stated above, extrapolation of the teachings of Stroganov regarding bone tissue growth stimulation by one of ordinary skill in the art would have resulted in exclusion of similar compositions in an endoprosthesis as claimed. Additionally, as stated previously, the Examiner's contention regarding Stroganov not excluding the possibility of use in inhibition of smooth muscle cell proliferation places a burden on the Applicants which the Examiner must properly bear regarding the establishment of obviousness of the claims. The Applicants are not required to rebut a case of obviousness over Stroganov unless and until the Examiner establishes a *prima facie* case that one of ordinary skill in the art would have found the claims obvious at the time of the invention. The Applicants maintain that the Examiner has not established such a *prima facie* case.

The Examiner has not established any suggestion or motivation, either in the reference itself or in the knowledge generally available to one of ordinary skill in the art, to modify the teachings of Stroganov to arrive at the present invention. That is, there is no suggestion or motivation for one of skill in the art to modify a bone growth-*stimulating* composition and to adapt it for use in blood vessels to *inhibit* smooth muscle proliferation. First, as mentioned above, one of ordinary skill in the art would understand that the general suitability of a composition with regard to treatment of bone would not be predictive of suitability of that same composition with regard to blood vessels. There must also be a reasonable expectation of success and the prior art reference or references must teach or suggest all of the claim limitations. (MPEP § 2143.)

As discussed above regarding claim 4, from which claims 9 and 12-14 depend, Stroganov does not provide any teaching or suggestion of the use of the composition in an endoprosthesis for implantation in vascular vessel or adaptation for intravascular liberation of the composition after implantation in a vascular vessel as claimed. Regarding the stated concentrations of the components of the alloy, the Examiner maintains it would be prima-facie obvious to combine two compositions taught by the prior art, to be useful for the same purpose, in order to form a third composition to be used for the same purpose. However, as stated above the purpose of Stroganov and the purpose of the present invention are very different. While Stroganov provides a bone screw composition to stimulate bone tissue growth, the present invention provides an endoprosthesis for intravascular placement and inhibition of smooth muscle cell growth. As also stated previously, Stroganov clearly provides an upper limit of total rare earth metals of 4.0 % by weight (column 2, line 21) while the claimed invention provides a total rare earth weight percentage (yttrium plus non-yttrium rare earths such as neodymium) of 5.2 % (claim 12), 5.5 % (claim 13), or 6.3% (claim 14).

Finally, the Applicants reiterate their argument that the lapse of 30 years between the issue date of Stroganov (29 August 1972) and the priority date of the present invention (13 November 2002), additionally demonstrates that the modification of Stroganov as suggested by the Examiner was not obvious to one of ordinary skill in the art at the time of the invention, despite well-publicized efforts to improve therapy for heart disease during this time period. For these reasons, claims 9 and 12-14 patentably distinguish over Stroganov. Withdrawal of the rejection of these claims under 35 U.S.C. § 103(a) is respectfully requested.

Claims 4 and 7 stand rejected as obvious over Heublein. The Examiner maintains that Heublein discloses a medical implant essentially as claimed except for the combination of

zirconium or neodymium with a magnesium carrier. It was further maintained that such an inclusion would have been obvious to one of ordinary skill in the art as a matter of routine experimentation in optimizing the properties of the resulting composition. However, to establish obviousness, there must be some teaching, suggestion, or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings. (MPEP § 2143). Additionally, the references must be must be considered as a whole and must suggest the desirability and thus the obviousness of making the combination. (MPEP § 2141). When Heublein is considered as a whole, the modification alleged by the Examiner can only be the result of impermissible hindsight.

The Examiner indicates that because Heublien provides vessel implants which over come the restenosis problems of permanent implants, Heublein therefore also provides stents adapted to inhibit smooth muscle cell proliferation. However, one of ordinary skill in the art would not equate a lack of stimulation of smooth muscle cell growth (achieved by the temporary presence of a degradable stent) with actual inhibition of smooth muscle cell proliferation. Heublein clearly does not contemplate the inhibition of smooth muscle cell proliferation as a property of the disclosed alloy.

The compositions disclosed in Heublein include a wide variety of potential components but Heublein provides no actual guidance as to advantages or disavantages of any of them, including inhibition of smooth muscle cell growth. For example, Heublein provides as potential components of the stent "pure iron," alloys or sintered metals having a main constituent selected from the group of alkali metals, of alkaline earth metals, iron, zinc or aluminium. (paragraph 0013). At least 23 possible "subsidiary constituents" of the alloy are also indicated (paragraph

0014). "Other metals and rare earths" are also disclosed as potential components (paragraph 0016). Furthermore, Heublein clearly indicates that a magnesium alloy containing up to 40 % lithium is preferred (paragraph 0014). Clearly, one of ordinary skill in the art would not consider such a diverse group of alloys to all inhibit smooth muscle cell proliferation in the absence of a clear teaching of such an effect. Therefore, one of ordinary skill in the art would not find any suggestion or motivation, either in Heublein or in the knowledge generally available to one of ordinary skill in the art, to modify Heublein to arrive at the invention recited in claims 4 and 7. For this reason, these claims patentably distinguish over Heublein. Withdrawal of the rejection of claims 4 and 7 under 35 U.S.C. § 103(a) is respectfully requested.

Claims 9 and 15 stand rejected as being obvious over Heublein as applied to claims 4 and 7 and in further view of The Columbia Electronic Encyclopedia, 6th Edition, 2007. The remarks made above regarding the distinctions between Heublien and claims 4 and 7 are repeated herein with regard to claims 9 and 15. Additionally, neither reference provides a teaching or suggestion of delivery of yttrium to the smooth muscle cells in the range of 200 μM and 2 mM as recited in claim 15. While the Examiner maintains that one of skill in the art would expect delivery of yttrium in this range by Heublein's composition, it should be noted how tenuous such a connection really is. First, as discussed above, rare earth elements are only generally disclosed by Heublein as one of many potential components. Additionally, yttrium is not specifically disclosed itself, although other rare earth elements are disclosed. Yttrium is only a possible component as one of the generally disclosed rare earth elements. The Examiner must rely on The Columbia Electronic Encyclopedia for the teaching that yttrium is a rare earth element. Furthermore, the actual concentration of yttrium delivered will depend on the rate of degradation of the overall alloy containing the yttrium. Neither of the cited references provides one of

ordinary skill in the art with any guidance on the desirability of delivery of yttrium at all, much less at the specified concentrations. Therefore, one of ordinary skill in the art would have had no reasonable expectation of success claims 9 and 15 patentably distinguish over Heublein in view of The Columbia Electronic Encyclopedia. Withdrawal of the rejection of claims 9 and 15 under 35 U.S.C. § 103(a) is respectfully requested.

The outstanding Office Action was electronically transmitted on 19 March 2009. The Examiner set a shortened statutory period for reply of 3 months from the mailing date. Therefore, no petition for an extension of time in making this response is believed to be due. However, the Applicants hereby make a conditional petition for any extension of time for response in the event that such a petition is required. The Commissioner is authorized to charge any fee required with this paper or to credit any overpayment to Deposit Account 15-0450.

Respectfully submitted,

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